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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/641,104	08/17/2000	Walter Birchmeier	0107-028P	5225
23622	7590	02-21-2003		
GABRIEL P. KATONA GOODWIN PROCTER L.L.P. 599 Lexington Avenue 40TH FLOOR NEW YORK, NY 10022			EXAMINER KAM, CHIH MIN	
			ART UNIT 1653	PAPER NUMBER 19
DATE MAILED: 02/21/2003				

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	09/641,104	BIRCHMEIER ET AL.
	<b>Examiner</b> Chih-Min Kam	<b>Art Unit</b> 1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### **Status**

- 1) Responsive to communication(s) filed on 29 November 2002.
- 2a) This action is **FINAL**.                  2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### **Disposition of Claims**

- 4) Claim(s) 9-19 and 29-43 is/are pending in the application.
- 4a) Of the above claim(s) 9-19 and 29-38 is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 39-43 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### **Application Papers**

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.  
 If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

#### **Priority under 35 U.S.C. §§ 119 and 120**

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
 \* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
 a)  The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### **Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                             | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____                                    |

## **DETAILED ACTION**

### ***Status of the Claims***

1. Claims 9-19 and 29-43 are pending.

Applicant's amendment filed on November 29, 2002 (Paper No. 18) is acknowledged.

Applicants' response has been fully considered. Claims 1-8 and 20-28 have been cancelled, claims 9-19 and 29-35 are non-elected invention, thus withdrawn from consideration. New claims 29-36 (applicants' numbering in Paper No. 18) have been added, where the numbering of claims 29-36 have been changed to claims 36-43 according to 37 C.F.R. 1.126. The newly added claims 36-38 are directed to non-elected amino acid sequences (SEQ ID NOs: 1, 2, 3 and 4) and withdrawn from consideration. Thus, claims 39-43 and SEQ ID NOs: 6, 7, 8, 9, 10, 11 and 12 are examined.

### ***Oath/Declaration***

2. The oath or declaration is defective as indicated in the previous Office Action. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because the oath is not dated by the inventors, Walter Birchmeier and Jens-Peter Von Kries.

### ***Abstract***

3. The newly submitted abstract in Paper No. 18 is acknowledged.

**Objection Withdrawn**

4. The previous objection to the specification regarding using one letter abbreviation for amino acid sequences and not citing the sequence identifier “SEQ ID NO:”, is withdrawn in view of applicants’ amendment to the specification in Paper No. 18.
5. The previous objection to claim 20, is withdrawn in view of applicants’ cancellation of the claim in Paper No. 18.

**Rejection Withdrawn**

***Claim Rejections - 35 USC § 112***

6. The previous rejection of claims 1-8 and 20-28 under 35 USC § 112, first and second paragraphs, is withdrawn in view of applicants’ cancellation of the claim in Paper No. 18.

***Informalities***

The disclosure is objected to because of the following informalities:

7. The drawings (Figs. 1-6) and Tables 1-2 are described in German instead of English. Appropriate correction is required. Applicants also submit Tables 3 and 4 as part of specification, however, there is no description on Tables 3 and 4, and appropriate clarification is required.
8. At page 11, in the description of Fig. 2, the word “analine” is misspelled. Appropriate correction is required. Applicant’s request for the substitution of “phenyl alanine” with “phenylalanine” on page 11 is not entered because applicant does not indicate the exact location of the changes (the line number) to be made, nor provides a clean copy of the amendment.

***Claim Objections***

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9. Claim 39 is objected to because the claim recites, for example, "SEQ. ID. NO.: 1" instead of "SEQ ID NO: 1".
10. Claim 43 is objected to because the claim recites "Arg. 386" in line 4. Use of "Arg 386" is suggested.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 36-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a peptide from armadillo domains of β-catenin (arms 3-9; SEQ ID NOS: 6, 7, 8, 9, 10, 11 and 12) which affect the interaction between β-catenin and LEF-1/TCF-4 (transcription factor), or between β-catenin and APC or conductin (tumor suppressor protein); or specific mutants of these armadillo peptides of β-catenin (arms 3-8) which have residue 253, 274, 338, 383, 469 or 470 substituted by Ala, does not reasonably provide enablement for an undefined mutant of a β-catenin armadillo peptide (arms 3-9) which affects the interaction between β-catenin and a transcription factor, or between β-catenin and a tumor suppressor protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 36-43 encompass an armadillo peptide of β-catenin (arms 3-9; SEQ ID NOS: 6, 7, 8, 9, 10, 11 and 12), or a mutant thereof, which affects the interaction between β-catenin and a

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transcription factor, or between β-catenin and a tumor suppressor gene product. The specification, however, only discloses cursory conclusions (pages 1 and 3) without data supporting the findings, which states that the invention relates to agents for treating human illness such as cancers based on the agents which can affect the interaction between β-catenin and transcription factors or tumor suppressor gene products, and these agents can be peptides derived from β-catenin. There are no indicia that the present application enables the full scope in view of armadillo peptides of β-catenin or mutants thereof as discussed in the stated rejection. The present application provides no indicia and no teaching/guidance as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breath of the claims, the absence of working examples, the state of the prior art and relative skill of those in the art, the unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breath of the claims:

The breath of the claims is broad and encompasses unspecified variants regarding the mutants of armadillo peptides of β-catenin, which are not adequately described or demonstrated in the specification.

(2). The absence of working examples:

There are no working examples indicating the claimed variants except for the armadillo peptides of β-catenin (arms 3-9) and the specific mutants of these armadillo peptides (Ala substituents at specific positions).

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(3). The state of the prior art and relative skill of those in the art:

The prior art (WO 98/42296) indicates compounds that interact with stabilized  $\beta$ -catenin or LEF can be identified through the determination of the binding regions of  $\beta$ -catenin or LEF by experimentation or molecular modeling, however, such compounds have not been specified. The general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on the identification of various mutants of armadillo peptides of  $\beta$ -catenin to be considered enabling for variants.

(4). Predictability or unpredictability of the art:

The claims encompass armadillo peptides of  $\beta$ -catenin or mutants thereof, which affect the interaction between  $\beta$ -catenin and a transcription factor or a tumor suppressor gene product, the invention is highly unpredictable regarding the amino acid sequences and the effects of these mutants.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to armadillo peptides of  $\beta$ -catenin or mutants thereof which affect the interaction between  $\beta$ -catenin and a transcription factor or a tumor suppressor gene product. The specification indicates some basic (Lys, Arg, His) or some aromatic amino acids in the armadillo repeat units 3-9 of  $\beta$ -catenin can be mutated to Ala (pages 6-7; Fig. 5), and several critical amino acid residues of  $\beta$ -catenin which affect the interaction with LEF-1/TCF, APC, conductin or E-cadherin are identified (Figs 5 and 6; Table 2; pages 9-10). However, the specification fails to identify any other mutants besides the Ala substituents at specific positions

of armadillo peptides of  $\beta$ -catenin (arms 3-9). Moreover, the specification has not shown any other mutants with different amino acid sequences can affect the interaction between  $\beta$ -catenin and a transcription factor or a tumor suppressor gene product. There are no working examples indicating various mutants of armadillo peptides of  $\beta$ -catenin can affect the interaction between  $\beta$ -catenin and a transcription factor or a tumor suppressor gene product. Furthermore, the specification does not provide any specific guidance on how to identify functional mutants of  $\beta$ -catenin armadillo peptides. Since the specification fails to provide sufficient guidance on the mutants of  $\beta$ -catenin armadillo peptides, it is necessary to carry out further experimentation to assess the effects of various mutants of armadillo peptides of  $\beta$ -catenin.

(6). Nature of the Invention

The scope of the claims encompasses armadillo peptides of  $\beta$ -catenin, or mutants thereof, however, the specification does not show how to identify various mutants of armadillo peptides of  $\beta$ -catenin besides the specific Ala substituents at specific positions. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, while the working example does not demonstrate the claimed variants, the art is unpredictable regarding the claimed variants, and the guidance and the teaching in the specification are limited, therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the effects of the mutants of armadillo peptides of  $\beta$ -catenin.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 39-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

13. Claims 39-43 are indefinite because of the use of the term “derived from” or “mutants”. The term “derived from” or “mutants” renders the claim indefinite, it is unclear how different the peptide derived from the armadillo domain of  $\beta$ -catenin is from the parent compound. Use of “obtained from” is suggested. It is also unclear what amino acid sequences the mutants have, e.g., which amino acid residues are mutated, and what amino acid residues are used for mutation. Claims 40-43 are included in the rejection because they are dependent on a rejected claim and do not correct the deficiency of the claim from which they depend.

14. Claim 41 is indefinite because of the use of the term “AP 20 amino acid repeats”. The term “AP 20 amino acid repeats” renders the claim indefinite, it is unclear what AP 20 amino acid repeats are.

15. Claims 42 and 43 are indefinite because the claim recites amino acid position(s) (e.g., His 470) without reference to an amino acid sequence identified with “SEQ ID NO:”. It is not clear what the amino acid position is without a sequence identifier “SEQ ID NO:”. Claims 42 and 43 are also indefinite because the claim recites, for example, “a peptide with a mutation in His 470”, it is not clear what peptide is intended, and what amino acid residue is used for mutation at His 470.

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***Conclusion***

16. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, Ph. D. can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. *CK*  
Patent Examiner

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February 18, 2003

*Karen Cochran Carlson, Ph.D.*

KAREN COCHRANE CARLSON, PH.D.  
PRIMARY EXAMINER